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Original Article

Is the Surgical Approach Very Important to Treatment for Phyllodes Tumors?

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Keywords: Malignant phyllodes tumor; recurrence; treatment.

ABSTRACT

Objective: The aim of the present study was to evaluate the treatment modalities and recurrence status of patients diagnosed with phyllodes tumor in light of a literature search.

Methods: All female patients who received treatment for phyllodes tumor between January 2015 and January 2017 were included in our study. All data were collected through retrospective analysis. Histopathological results, type of surgery, application of chemoradiotherapy, tumor size, recurrence rate, and demographic data were analyzed.

Results: Twenty-five cases were evaluated. Of the 25 cases, 8 were diagnosed as malignant. The rest were 3 borderline and 14 benign and fibroadenomas. Three of 8 malignancies were treated with mastectomy, and the other 5 were treated with wide local excision. Recurrence occurred in two cases; one of them received chemotherapy, and the other had chemoradiotherapy. All 17 remaining patients underwent wide local excision. A single case was treated with mastectomy due to large tumor size.

Conclusion: There is still an ongoing debate for the treatment of phyllodes tumors. Negative margins for malignant cases play a major role for successful treatment. There is no consensus for the application of chemo- and radiotherapy.

INTRODUCTION

Breast tumors remain as one of the major health problems with increasing incidence, especially for females.[1] Phyllodes tumors are encountered very rarely. They represent 2% of all fibroepithelial tumors and 0.1%–0.3% of all breast masses.[2] After all discussions about the classification of phyllodes tumors, recently, the World Health Organization published a consensus criteria in 2003 indicating phyllodes tumors as benign, borderline, and malignant.[2]

Local recurrence is a very important problem for the successful treatment of phyllodes tumors. Literature review reveals a local recurrence rate >40% for all pathological types.[3] Delay of suitable treatment increases the possibility of distant metastases due to rapid progression. Tumor spreads usually via the bloodstream, but rarely lymph nodes may play a small role. The most frequent sites for metastases are the lung, soft tissue, bone, and pleura.[4] The rate of metastases is 25%–31% for malignant and borderline tumors, whereas 4% for all types of phyllodes masses.[5]

Despite core biopsies, absolute diagnosis of phyllodes tumors remains to be very difficult. Moreover, there is still a contradiction in oncological treatment of these tumors.[6] Therefore, advanced diagnosis techniques and suitable treatment modalities are required.

We tried to evaluate the treatment modalities and recurrence status of patients diagnosed with phyllodes tumor in light of a literature search.

MATERIALS AND METHODS

All female patients who received treatment for phyllodes tumor between January 2015 and January 2017 were included in our study. All data were collected through retrospective analysis.

Demographic data (age, gender, and body mass index), radiological data (size and localization), results of tru-cut and excisional biopsy, type of surgery, adjuvant oncologic therapy methods, postoperative follow-ups, and recurrence and survival rates were retrospectively analyzed. Patients with an American Society of Anesthesiologists score of IV and incomplete data were excluded from the study.

Table 1. Clinical data according to pathological results

	No. of patients	Wide local excision	Mastectomy	CT+RT	CT	Recurrence	Exitus
Malignant phyllodes	8	5	3	1	1	2	2
Borderline phyllodes	3	2	1	–	–	–	–
Benign phyllodes and fibroadenoma lesions	14	14	–	–	–	–	–
Total	25	21	4	1	1	2	2

CT: Chemotherapy; RT: Radiotherapy.

Statistical analysis

Parametric data were evaluated using Student's t-test, whereas non-parametric data were evaluated using Fisher's exact or Pearson's chi-squared test. A P value <0.05 was considered as statistically significant.

RESULTS

Thirty patients were diagnosed with phyllodes tumor, five of them were excluded due to incomplete data. All cases were females with a mean age of 36.6±11.8 years. According to radiological data, all tumors were solitary. The mean diameter of tumors was 5.5±2.8 cm. Localizations for tumors were as follows: 14 (56%) left breast, 11 (44%) right breast. Tru-cut biopsies revealed 3 (12%) benign, 3 (12%) phyllodes tumor, 17 (68%) fibroepithelial lesion, 1 (4%) fibroepithelial lesion with suspected malignancy, and 1 malignant tumor. The mean size for malignant tumors was 6.3±3.3 cm.

At the first operation, 7 out of 8 patients with malignancies received wide local excision, and the other one had mastectomy. A single case of wide local excision received chemotherapy (CT) due to a surgical margin <1 cm. This patient had local recurrence and multiple metastases at the lung and bones after 6 months and died at month 10 after surgery. Another patient who received wide local excision had adjuvant chemoradiotherapy due to a surgical margin <1 cm. This patient underwent total mastectomy after 6 months due to local recurrence. A patient was lost at month 7 because of distant metastases. Another patient received early mastectomy due to a margin closer than 1 mm. Fortunately, this case had neither recurrence nor metastasis. The remaining five patients with malignant phyllodes tumor had no metastasis or recurrence within 37 months following surgery (Table 1).

One patient diagnosed with borderline phyllodes tumor received mastectomy due to the size of tumor and was implanted an expander (Fig. 1a–c). The other two patients underwent wide local excision. There was no requirement for chemoradiotherapy. No recurrence or metastasis was detected through 40 months of follow-up.

All cases diagnosed with benign phyllodes tumor received wide local excisions, and again no recurrence was found within 40 months. Unfortunately, one patient died due to sarcoidosis within 24 months.

DISCUSSION

Of all breast tumors, <1% was diagnosed as phyllodes tumors.[7,8] Owing to the limited presence of these types of tumors, shortage of epidemiological data remains a major obstacle for successful treatment. In 17 years of analysis in Los Angeles, the mean incidence of phyllodes tumors was 2.1/1,000,000/year. Latin people suffer more frequently.[9] Phyllodes tumors occur in women, with a median age at presentation of 42–45 years.[2,9–11] Malignant phyllodes tumors are usually seen in older ages.[12] The mean age in our study was 36.6 years, and the median age was 39 years, whereas it was 46 years for patients with malignancy. We found similar results with the literature.

The main complaint for phyllodes tumors is palpable mass in the majority of cases. A limited number of patients are

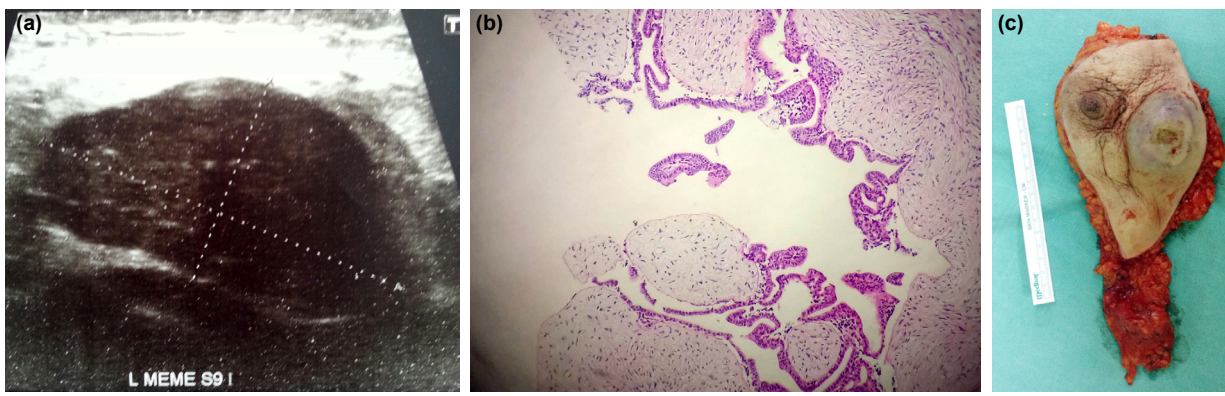

Figure 1. Phyllodes tumor. **a)** Radiological appearance, **b)** microscopic wiew, **c)** macroscopic wiew.

diagnosed by ultrasound or mammography. Macdonald et al. reported, including SEER data, that 20% of all phyllodes cases are diagnosed via screening mammographies.[13] In our study, all tumors were palpable. These tumors were mostly soft, multinodular, mobile, district margins and painless. There is a wide range for tumor size. Literature review reveals even masses >41 cm, usually mean size is 4–7 cm.[7,11] We found similar results, the mean size in our study was 6.3 cm.

There is no special growth pattern for phyllodes tumors. Some cases grow gradually, whereas some grow very slowly. Some cases may show biphasic growth pattern. Large tumors may have disrupt breast contour and even can cause necrosis in the skin due to pressure.

In 20% of all cases diagnosed as phyllodes tumor, axillary lymph nodes could be palpable. However, the majority of these nodes are considered as reactive. Metastatic lymph nodes are rarely seen. Therefore, axillary dissection is not required routinely.[13] According to SEER data, only 8 out of 498 patients showed signs of invaded lymph nodes. In our study, there was no lymph node involvement, and we did not apply axillary dissection.

Fine needle biopsies are usually insufficient due to high false negative rates.[14] In addition, we did not utilize these types of biopsies in our study.

Core biopsies play a major role in diagnosing phyllodes tumors; however, 25%–30% of false negative results were reported.[15,16] In our series, the rate for definitive diagnosis was 88%.

Histologically, phyllodes tumors are classified as benign, borderline, and malignant according to the grade of cellular atypia, mitotic activity, and margins of tumor.[7,9,10,17,18] In our study, 8 (32%) cases were malignant, 3 (12%) borderline, and 14 (56%) benign, respectively.

The gold standard therapy for phyllodes tumors is total excision. A margin >1 cm is required with low rates of recurrence.[7,19–21] In a multivariate analysis with 172 patients, insufficient margins play a major role in the occurrence of local recurrence and metastases.[22] Sotheran et al.[23] are in favor of wide local excision for phyllodes tumors, whereas Hassouna et al.[24] recommend mastectomy. Kapris et al.[25] found no difference between wide local excision and mastectomy, in case of negative margins. Pandey et al.[26] described positive margins as an independent risk factor for recurrence. We were able to maintain sufficient margins in our series, except for one case. This patient received mastectomy thereafter. Local recurrences for benign, borderline, and malignant phyllodes tumors were 8%, 21%, and 36%, respectively.[19,27] However, recent studies report lower rates (6.3% out of 479 patients).[28]

In case of recurrence, reoperations and radiotherapy (RT) are advised. RT should be applied for cases with insufficient margins. There is still an ongoing debate for the application of RT for negative margins. Jacklin et al.[14] reported that RT may control local tumors for 10 years but does not have an effect on survival. Pandey et al.[26] described the positive effects of RT on survival. Barth et al.[19] reported that RT after breast conserving surgery decreases local recurrence. Mituś et al.[6] found no difference between breast conserving surgery with negative margins and surgery with suspected margins and RT according to survival. They believe that adjuvant RT should be applied for cases with margins <1 cm. In MD Anderson Center for Cancer, in case of medical inoperability, RT is usually advised.[15] There is no consensus on the advantages of RT in cases who received total excision of tumors. We applied RT to one patient with local recurrence.

Literature review reveals no randomized study for specific adjuvant CT in phyllodes tumors. The application of CT remains limited due to the lack of sufficient data. One study with 28 malignant phyllodes tumors found no difference between CT (doxorubicin+dacarbazine) and surgery.[29] Zhou et al.[30] advise that stromal cell atypia, mitotic activation, and histological grade should play a decisive role for CT. In light of these limited data, adjuvant CT is only suitable for selected high risk cases (recurrence and tumor size >10 cm). In case of systemic CT, soft tissue regimens should be applied. The effects of hormonotherapy are not well-known.[8,31]

Recurrence in phyllodes tumors usually occurs within a period of 2 years local surgery.[4,8] In some studies, time until recurrence is shorter for malignant tumors than for benign and borderline masses. In some cases, benign tumors may show atypical cells at recurrence sites. In a study including 293 cases, recurrence of six benign tumors were malignant.[11]

Treatment modality for recurrent phyllodes tumors is re-excision and RT. For unresectable cases, RT is the only option.[32] There were two cases with recurrences in our study. These two cases were diagnosed as malignant. One patient had undergone CT, and the other had mastectomy and chemoradiotherapy. Both patients died due to distant metastases.

Rates of metastases for phyllodes tumors are between 13% and 40%.[1,2,4,14] General survival is approximately 30 months.[33] The most frequent site for metastasis is the lungs. Metastatic lesions are usually >5 cm and include structures of malignant phyllodes tumors. The current approach for metastatic lesions is surgical excision. Chemotherapeutic regimens for soft tissue sarcoma could be applied for these metastases. In our study, two cases had distant metastases. Both cases had metastases following local recurrence. These metastases were not suitable for surgery; therefore, CT was applied. Unfortunately, both patients died at months 4 and 7.

The 5-year survival for phyllodes tumors is reported to be between 60% and 80% according to histological type. In a retrospective study including 70 patients, the 3-year survival for benign and borderline tumors was reported as 100%, whereas it was 54% for malignant masses.[34] In addition, in another study with 101 cases, the 5-year survival for benign/borderline tumors was 91%. For malignant

tumors, they reported this rate as 82%.[20] In our study, these rates were 93.8% and 70%, respectively.

CONCLUSION

There are various types of treatment modalities for phyllodes tumors. We believe that negative margins is necessary for successful treatment. There is no consensus for RT and CT applications. Future studies with more patients are required.

Ethics Committee Approval

Approved by the Kartal Dr. Lütfi Kırdar Training and Research Hospital Ethics Committee (date: 20.09.2017, number: 2017/514/144/3).

Peer-review

Internally peer-reviewed.

Authorship Contributions

Concept: M.F.K.; Design: M.F.K., H.F.K.; Data collection &/or processing: M.F.K.; Analysis and/or interpretation: K.Ç., S.K.; Literature search: K.Ç., S.K.; Writing: M.F.K.; Critical review: M.F.K.

Conflict of Interest

None declared.

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Filodes Tümörlerinde Cerrahi Yaklaşımın Önemi

Amaç: Filoides tümörü tanısı alan hastaların kliniğimizdeki tedavi ve nüks durumunu literatür eşliğinde irdelemek.

Gereç ve Yöntem: Ocak 2015 ile ocak 2017 tarihleri arasında fibroepitelyal tümör tanısı ile ameliyat edilen kadın hastalar dahil edildi. Veriler hasta dosyası incelenerek geriye dönük toplandı. Hastalar patoloji sonuçlarına göre yapılan ameliyat, kemoterapi ve radypterapi alıp almamaları, kitlenin büyüklüğü, nüks ve demografik özelliklerine göre değerlendirildi.

Bulgular: Toplam 25 hasta değerlendirildi. Bunlardan sekizi malign filoides tümör, üçü Borderline filoides tümör, 14'ü benign filoides tümör ve fibroadenomatoz lezyon idi. Sekiz malign filoides tümörlü hastanın üçüne mastektomi beşine geniş lokal eksizyon (GLE) yapıldı. İki hastada nüks gelişti. Bunlardan birisine kemoterapi (KT), diğerine KT ve radyoterapi (RT) uygulanmıştı. Diğer 17 hastadan biri hariç (kitle memeyi tamamen kapladığı için mastektomi yapıldı) hepsine GLE uygulandı.

Sonuç: Malign filoides tümör tedavisi için çeşitli görüşler bulunmaktadır. Ancak cerrahi sınır negatifliği ön plana çıkmaktadır. RT ve KT eklenip eklenmemesi halen tartışmalıdır.

Anahtar Sözcükler: Malign filoides tümör; nüks; tedavi.